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Clinical Evaluation of Safety and Efficacy of Vedistry Arjuna + Tablet in Hyperlipidemia

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Objective: To establish the efficacy and safety of Vedistry Arjuna + Tablet in the management of hyperlipidemia.

Methods: A randomized, double blind, active controlled, single center, clinical study was carried out using Vedistry Arjuna + Tablet for the duration of 12 weeks in 300 patients with hyperlipidemia and chronic stable angina.

Results: The results showed that Vedistry Arjuna + Tablet and Simvastatin both produced significant reduction of cholesterol and triglycerides. In addition, the group receiving Vedistry Arjuna + Tablet reported significant improvements in the stress test parameters compared to those receiving Simvastatin. Low incidences of side-effects in the Vedistry Arjuna + Tablet receiving group compared to Simvastatin receiving group indicates that Arjuna would be a safer alternative.

Conclusion: These findings suggest that Vedistry Arjuna + Tablet possesses antihyper-lipidemic, antihypertensive, and cardiac function improving activities.

Keywords: Hyperlipidemia, High cholesterol, Elevated lipids, LDL cholesterol (Low-Density Lipoprotein), HDL cholesterol (High-Density Lipoprotein), Triglycerides, Atherosclerosis, Cardiovascular disease

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Introduction

Cardiovascular diseases (CVDs) are the leading causes of morbidity and mortality in developed countries and are expected to result in over 23.6 million CVD-related deaths worldwide by 2030.**[1]** The World Health Organization (WHO) defines CVDs as a group of disorders of the heart and/or blood vessels which include hypertension (HT), coronary heart disease (CHD), cerebrovascular disease, peripheral arterial disease (PAD), cardiomyopathies, and heart failure.**[2]**

Elevated blood pressure, dietary risks, and lipid disorders, mainly hypercholesterolemia, are in terms of prevalence, the top three cardiovascular risk factors in the world.**[3]**

Lowering plasma cholesterol levels has been proven to significantly decrease the occurrence of coronary artery disease and stroke. Lipid-lowering therapy is the most efficacious approach to primary and secondary prevention of atherosclerotic cardiovascular disease (ASCVD). Lipid-lowering therapy in primary prevention is associated with a reduction in the risk of death from any cause by 11%, CV death by 20%, acute coronary syndrome by 38%, stroke by 17%, unstable CAD by 25% and major CV events by 26%.**[4]**

Herbs have a significant role to play in both diet and the treatment of diseases. Studies are currently being conducted to determine the lipid-lowering properties of various herbal plants described in Ayurveda texts. Clinical studies also have reported that Ayurvedic herbal medicines are effective in lowering LDL-C.**[5]**

Terminalia arjuna, commonly known as Arjuna, is a potential cardio protective agent belonging to the Combretaceae family. Many ancient Ayurvedic texts have prescribed it as an effective remedy for various cardiovascular disorders like anginal pain, hypertension, congestive heart failure, and dyslipidemia.**[6]** Stembark of Arjuna possesses diuretic, inotropic, and chronotropic properties.**[7]**

In a randomized, double-blind, cross-over study done in 58 male patients with chronic stable angina (class II–III), treatment with 500 mg of 90% alcohol extract of Arjuna 8 hourly, ISMN (40 mg/day), or a matching placebo for 1 week resulted in a significant decrease in the frequency of angina and the need for isosorbide dinitrate.

Improvements in clinical and TMT parameters were observed with both Arjuna and ISMN as compared to placebo.**[8]**

With the above leads we planned a double-blind comparative clinical study using Vedistry Arjuna + Tablet and Simvastatin.

Materials and methods

Study design

The present study was a randomized, double-blind, comparative clinical trial designed to evaluate the efficacy and safety of Vedistry Arjuna + Tablet and Simvastatin (used as the reference standard) in patients with chronic stable angina (NYHA class II-III), evidence of provocable ischemia on stress test, and hyperlipidemia. Vedistry Arjuna + Tablet was supplied by Charak Pharma Ltd, Mumbai. The study was Carried out at Dr. Neelam Chaturvedis' Shree Vishwadhatri Ayurved Clinic Mumbai, & Dr. Manoj Pandey, Shree Samarth Clinic, Mumbai India, from January 2024 to June 2024. All procedures were reviewed and approved by Principal Investigator. A total of 390 patients attending the medicine outpatient clinic were evaluated through medical history and physical examination. Patients with secondary hyperlipidemia, alcoholism, or body weight more than 15% above the ideal for their height were excluded from the study. Baseline cholesterol and triglyceride levels were measured. After screening, 300 patients with evidence of provocable ischemia on stress test and serum cholesterol levels exceeding 200 mg/dL or triglyceride levels over 200 mg/dl were selected.

The patients were randomly assigned to two groups using a randomization table: Vedistry Arjuna + Tablet (Group 1, n=150) and Simvastatin (Group 2, n=150). Informed consent was obtained from all participants, who were instructed to adhere to study protocols. Demographic data, detailed case history, including any previous diseases, and medication history were recorded, along with a physical examination.

Safety assessments included Liver Function Tests (LFTs) and Kidney Function Tests (KFTs), conducted on Day 0 and Day 84. Clinical side effects were recorded at each visit, and their nature, severity, and frequency were discussed with the patient. Routine haematological and urine analysis were also performed.

Patients were instructed to fast for 12-14 hours before blood samples were drawn. The study followed a double-blind, randomized comparative design over 12 weeks. Group 1 received one Vedistry Arjuna + Tablet twice daily after meals, while Group 2 received 40 mg of Simvastatin daily after meals. Patients were required to visit the clinic every two weeks throughout the 12-week study duration.

Preparation of Vedistry Arjuna + Tablet

Vedistry Arjuna + Tablet was procured from Charak Pharma Pvt ltd. Each tablet of Arjuna Plus contains *Arjuna* powder 250 mg, extract of *Arjuna* bark standardized to contain 250 mg and 25 mg of *Pippali* fruit extract triturated in *Arjuna Kwatha.*

Inclusion criteria

A total of 300 patients were selected based on signs, symptoms, and haematological changes consistent with the defined inclusion criteria. The patients were aged between 35 and 65 years, with a median age of 47. Among them, 235 were male, and 65 were female, all diagnosed with chronic stable angina (NYHA class II-III) with evidence of Provo cable ischemia on a stress test and hyper-lipidemia. Written and informed consent was obtained from all patients. All patients were interviewed by a registered dietician, who provided guidance on following a low-cholesterol and low-saturated fat diet. Throughout study, patients consistently met with same dietician at each clinic visit to receive dietary instructions. They were advised to maintain their weight, physical activity levels, and smoking frequency.

To evaluate dietary compliance, patients recorded quantity and type of food consumed over four consecutive days, including a weekend, between clinic visits. These food diaries were completed on special forms, which were subsequently translated into a computer-readable format and analysed by a dedicated program. Patients also reported their usual physical activity and smoking habits on a special card at each visit. Repeat laboratory investigations and electrocardiography were performed upon completion of the study. Concomitant medications were monitored throughout the study. Of the 300 patients, 210 did not take any other drugs, 20 took aspirin, 12 took anti-allergenic preparations, 35 took vitamins or mineral supplements, 10 took nonsteroidal The results were analysed using a paired 't' test to evaluate the changes from baseline.

Exclusion criteria

The exclusion criteria included patients with secondary hyperlipidemia, alcoholism, or body weight more than 20% above the ideal for their height, having uncontrolled Diabetes or diabetics on Insulin, arrhythmia, congestive cardiac failure, or history of angioplasty. Patients advised angioplasty were also excluded.

Efficacy and safety evaluation

The response of patients to stress test parameters and changes in serum cholesterol and triglyceride levels were evaluated. The stress test measures maximum exercise time in minutes, ST-segment depression, and time to recovery from ST Segment depression. Also, other parameters like heart rate and blood pressure were noted. The baseline values of these parameters were compared to that of the end of treatment (EOT) by employing appropriate statistical tools. Laboratory evaluations were performed to assess the safety through different biochemical parameters in serum and hematological analysis. None of the enrolled patients had an abnormal medical history. No abnormality in physical findings was observed on the screening visit or during the study visit. Statistical analysis was done using a paired 't' test.

Results

A total of 300 patients were accepted who met inclusion criteria after initial screening in study and randomized. A total of 268 patients completed study protocol. Patients from Simvastatin group dropped out due to personal / family issues and one patient from Vedistry Arjuna + Tablet was excluded because of non-compliance. The patients followed fairly uniform dietary patterns during trial and their compliance was assured by routine interviews with dietician and review of computer's analysis of dietary records at every clinic visit. Routine follow-up by dietician resulted in good overall dietary compliance.

Baseline characteristics

Table 1 illustrates the baseline characteristic of the patients prior to the intervention in the Vedistry Arjuna + Tablet and the Reference group.

There was no considerable difference between the groups in terms of the baseline characteristics in terms of age, weight, height and body mass index (BMI). Similarly, the two groups were not considerably different in respect of gender, pulse, respiration, temperature, systolic blood pressure and diastolic blood pressure.

Table 1: Comparison of baseline characteristics for the variable under investigation in Vedistry Arjuna + Tablet and Simvastatin groups.

Item	Vedistry Arjuna + Tablet (n=150)	Simvastatin (n=150)
Age (years)	47.0 ± 7.87	47.1 ± 7.91
Gender [n (%)]		
Male	105 (70%)	130 (86.7%)
Female	45 (30%)	20 (13.3%)
Weight (kg)	67.5 ± 15.16	66.8 ± 16.24
Height (cm)	156.7 ± 11.17	154.8 ± 10.48
BMI (kg/m²)	27.78 ± 6.16	27.62 ± 5.78
Pulse (beats/min)	78.3 ± 8.73	79.0 ± 6.89
Respiratory (/min)	20.9 ± 1.60	21.0 ± 1.57
Temperature (°F)	97.8 ± 1.25	97.9 ± 0.84
Systolic BP (mm/Hg)	138.9 ± 11.12	136.5 ± 8.68
Diastolic BP (mm/Hg)	89.0 ± 7.45	86.7 ± 5.61
Diagnosis	Chronic Stable Angina (NYHA Class II-III), Ischemia on Stress Test, Hyperlipidemia	Chronic Stable Angina (NYHA Class II-III), Ischemia on Stress Test, Hyperlipidemia
Concomitant Medications	No other drugs: 105, Aspirin: 7, Anti-allergenic: 4, Vitamins/Minerals: 6, NSAIDs: 3, Antacids: 5	No other drugs: 105, Aspirin: 13, Anti-allergenic: 8, Vitamins/Minerals: 9, NSAIDs: 5, Antacids: 5

Stress Test

The comparison of treatment effects on stress test parameters between the Vedistry Arjuna + Tablet group and the Simvastatin group is presented in Table 2. In the Vedistry Arjuna + Tablet group, significant improvements were observed in treadmill exercise test parameters after therapy. The total duration of exercise significantly increased to 6.14 ± 2.50 minutes, compared to 4.74 ± 2.34 minutes in the Simvastatin group ($p < 0.005$). Additionally, the maximal ST depression during the longest equivalent stages of submaximal exercise decreased from 2.20 ± 0.56 mm in the Simvastatin group to 1.40 ± 0.55 mm in the Vedistry Arjuna + Tablet group ($p < 0.005$). The time to recovery also improved, Decreasing to 6.48 ± 2.27 minutes in the Vedistry Arjuna + Tablet group, compared to 9.01 ± 3.40 minutes in the Simvastatin group ($p < 0.005$). No significant differences were observed in the stress test parameters of the Simvastatin group.

Table 2: Treatment effect of Vedistry Arjuna + Tablet and Simvastatin group as measured at baseline and day 84 on Stress Test.

Item	Vedistry Arjuna + Tablet		Simvastatin	
	0 Day	84 Day	0 Day	84 Day
The maximum exercise time	4.74 ± 2.34 mins	6.14 ± 2.50 mins*	5.10 ± 1.34 mins	5.28 ± 1.44 mins
ST-segment depression	2.20 ± 0.56 mm	1.40 ± 0.55 mm*	2.18 ± 0.24 mm	2.14 ± 0.14 mm
Time to Recovery from ST Segment Depression	9.01 ± 3.40 mins	6.48 ± 2.27 mins*	9.32 ± 2.40 mins	8.21 ± 3.37 mins
Blood Pressure				
Systolic BP (mm/Hg)	138.9 ± 11.12	129.45 ± 9.32*	136.5 ± 8.68	135.45 ± 4.58
Diastolic BP (mm/Hg)	89.0 ± 7.45	86.47 ± 10.25	86.7 ± 5.61	85.35 ± 6.18
Pulse Rate (per min)	82.46 ± 3.68	76.46 ± 4.24*	81.38 ± 2.88	80.26 ± 4.82
*p<0.005 as compared to the before treatment value				

Changes in the lipid levels

Comparison of the treatment effect on the cholesterol, triglycerides, HDL, LDL, VLDL in Vedistry Arjuna + Tablet and reference group are given in Table 3. Results of those patients taking Arjuna Plus showed a reduction of cholesterol from 223.30 ± 5.42 mg/dl to 193.50 ± 9.10 mg/dl. Reduction in cholesterol from 215.47 ± 8.43 to 177.00 ± 7.55 mg/dl occurred with Simvastatin. Serum triglycerides levels were also reduced from 218.00 ± 22.37 mg/dl to 188.70 ± 22.28 mg/dl and 219.70 ± 24.09 to 183.5 ± 21.63 mg/dl with Arjuna Plus and Simvastatin respectively. In HDL, levels were increased in a similar fashion with Arjuna Plus and Simvastatin treatment. Although the rise in HDL cholesterol was similar in both the drugs, Simvastatin produced an increase of HDL-cholesterol marginally higher than the Arjuna Plus. Similarly, more significant reduction in VLDL cholesterol was observed in Simvastatin group (from 42.93 ±5.47 to 33.85 ± 5.68 mg/dl) compared to Vedistry Arjuna + Tablet (40.57 ± 3.43 to 39.53 ± 4.16 mg/dl). Thus, both Arjuna Plus and Simvastatin reduced the cholesterol, triglycerides, LDL and VLDL levels and increased HDL cholesterol levels.

The analysis of both drugs shows the reduction of cholesterol, triglycerides, LDL and VLDL in comparative manner.

Table 3: Summary of mean change from baseline to end of treatment in lipid levels

Clinical parameters	Vedistry Arjuna + Tablet		Simvastatin	
	0 Day	84 Days	0 Day 0	84 Days
Cholesterol (mg/dl)	223.30 ± 5.42	193.50 ± 9.10*	215.47 ± 8.43	177.00 ± 7.55*
Triglycerides (mg/dl)	218.00 ± 22.37	188.70 ± 22.28*	219.70 ± 24.09	183.5 ± 21.63*
HDL (mg/dl)	38.50 ± 2.54	41.65 ± 1.83	38.25 ± 3.10	41.85 ± 2.05
LDL (mg/dl)	132.80 ± 6.07	114.60 ± 7.45*	128.10 ± 7.90	98.95 ± 5.45*
VLDL (mg/dl)	40.57 ± 3.43	39.53 ± 4.16*	42.93 ±5.47	33.85 ± 5.68*
*p<0.001 as compared to the before treatment value				

Biochemical Parameters

Parameters of Liver Function Test and Kidney Function Tests were analyzed at day 0 and day 84 to evaluate safety of treatment. The results of biochemical parameters of blood tests are given in Table 4. In the Arjuna Plus group, they remained within normal ranges throughout the study and no patient demonstrated an abnormal health issue which required further medical consultation or treatment. But in the Simvastin receiving group, a borderline increase in Liver Function test parameters was observed. There was no significant change in the general health condition of the patients in both treatment groups.

Table 4: Summary of mean change from baseline to end of treatment in biochemical parameters

Parameters	Vedistry Arjuna + Tablet		Simvastatin	
	Day 0	Day 84	Day 0	Day 84
Albumin (g/dl)	4.16 ± 0.37	4.38 ± 0.31	4.23 ± 0.38	5.23 ± 0.31
Total bilirubin (mg/dl)	0.66 ± 0.18	1.69 ± 0.11	0.66 ± 0.18	1.55 ± 0.11
SGOT (U/L)	19.50 ± 4.87	19.20 ± 0.13	19.77 ± 4.87	22.17 ± 3.86
SGPT (U/L)	23.04 ± 8.0	22.92 ± 3.8	23.4 ± 8.0	26.9 ± 3.86
Uric acid (mg/dl)	5.6 ± 0.9	5.3 ± 1.02	5.1 ± 0.9	5.9 ± 1.0
Total Protein (gm/dl)	7.0 ± 0.8	7.3 ± 0.8	7.2 ± 0.8	8.4 ± 0.8
BUN (mg/dl)	16.50 ± 4.68	12.21 ± 4.9	15.76 ± 4.68	17.01 ± 4.9
Serum Creatinine (mg/dL)	0.84 ± 0.18	0.77 ± 0.01	0.77 ± 0.18	0.89 ± 0.01
Leucocyte count (cells/µL)	8880.95 ± 1819.91	8085 ± 1729.16	8858.33 ± 1819.91	8308.69 ± 1729.16
ESR (mm)	25.28 ± 11.90	21.3 ± 9.17	23.83 ± 11.90	24.73 ± 9.17

Discussion

High serum cholesterol is regarded by many as main cause of coronary atherosclerosis.**[9]** Several cholesterol lowering interventions have reduced coronary heart disease (CHD) events in primary and secondary prevention clinical trials.**[10]**

Even expert panels in Europe and USA have therefore recommended dietary changes and, if necessary, addition of drugs to reduce high cholesterol concentrations especially low-density-lipoprotein (LDL) cholesterol**[11]** especially in patients with CHD.

Statins are one of most widely used drugs worldwide as first-line drugs for treatment of hyperlipidemia and prevention and treatment of cardiovascular diseases. In 2019, ACC/AHA issued revised guidelines on primary prevention of cardiovascular disease. It recommends initiation of statin therapy in persons with 10-year risk ≥7.5% ("intermediate" or "high") and a risk discussion in persons at 5% to <7.5% ("borderline") risk.**[12]** Statins can favorably affect course of chronic stable angina presumably by halting or reversing plaque buildup responsible for vessel stenosis.**[13]**Statins, though well tolerated, are found to be associated with certain skeletal muscle, metabolic, and neurological side effects. Various side effects like hepatotoxicity, muscle disease, acute renal failure, cataracts, and an increased risk of diabetes mellitus, have been reported in statin users.**[14]**

Complementary and alternative therapies have long been used in Eastern world but recently these therapies are being used increasingly worldwide. When conventional medicine fails to treat chronic diseases and conditions efficiently and without adverse events, it is not unlikely that many people seek unconventional therapies such as herbal medicine. **[15]** Many herbs have been used in Ayurvedic medicine for more than three millennia for treating various cardiovascular ailments. Arjuna has been used primarily as a cardiac tonic.

This clinical study was undertaken to evaluate efficacy as well as safety of Vedistry Arjuna + Tablet which contains Arjuna powder- 250 mg, extract of Arjuna bark - 250 mg and 25 mg of Pippali fruit extract triturated in Arjuna kwatha.Arjuna is known to be useful in alleviating anginal pain,hypercholesterolemia, heart failure, and coronary artery disease.

It has been shown in animal studies and clinical trials to have cardio tonic, antihypertensive, antihyperlipidemic, antioxidant, and anticoagulant properties. Among the bioactive constituents in Arjuna are tannins, triterpenoid saponins, flavonoids, gallic acid, ellagic acid, oligomeric proanthocyanidins, phytosterols, and several minerals (calcium, magnesium, zinc, and copper). The antioxidant cardioprotective effects are attributed to flavonoids and oligomeric proanthocyanidins; the positive inotropic effects may be caused by saponin glycosides. **[16]** *Pippali* extract contains piperine which is known to enhance the bioavailability and efficacy of medicinal herbs. **[17]** This ensures efficient absorption and utilization of Arjuna extract to give maximum benefits.

Our findings show Arjuna Plus is efficacious in not only lowering serum cholesterol, triglyceride, LDL levels without causing any side effects but also enhancing cardiac function as evident from improved Stress Test parameters. Also the biochemical tests showed that all the parameters were within normal limits before and after treatment proving safety of Vedistry Arjuna + Tablet. Though Simvastatin significantly reduced cholesterol and triglyceride levels no significant improvement was observed in Stress Test parameters. Also, there was a slight increase in the liver function tests. This shows that Vedistry Arjuna + Tablet can serve dual benefits of lowering lipid levels and improving cardiac function too without any side effects.

Conclusion

According to results of this study, Arjuna Plus and Simvastatin both produce significant reduction of cholesterol and triglycerides. The fact that the Simvastatin group had marginally increased incidence of side-effects and no significant improvement in cardiac function, Vedistry Arjuna + Tablet would be a safer alternative. Thus This Study Concludes that, Arjuna+ Tablet reduces Cholesterol and Lipids and Improves Lipid Metabolism and Overall Metabolism, Work as Cardiac Tonic.

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